Calmodulin transduces Ca^{2+} oscillations into differential regulation of its target proteins

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Supplementary information

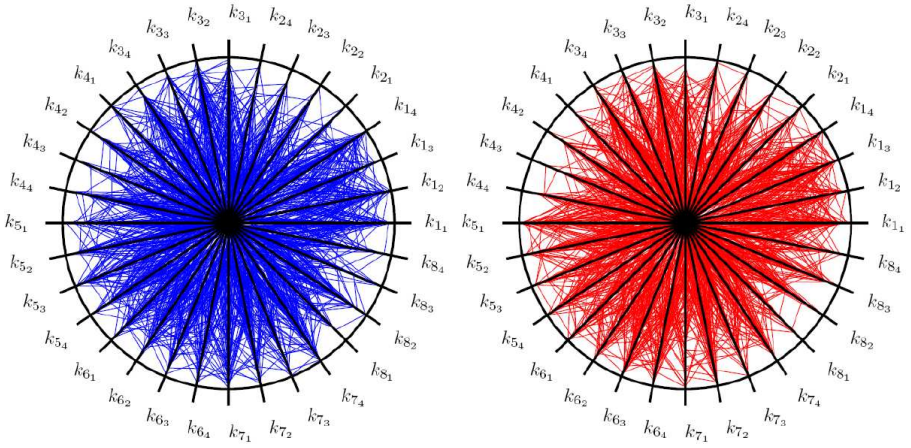
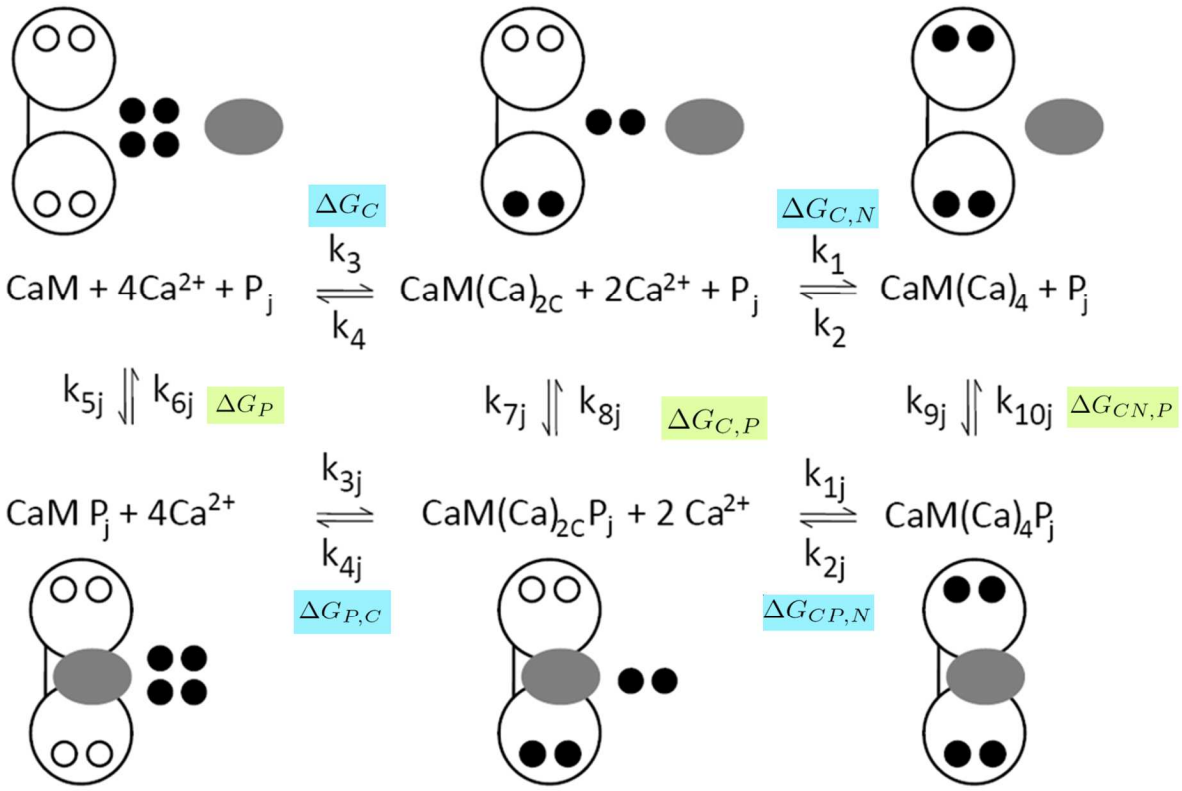


Figure S1. Sets of rate constants yielding the 100 lowest (left, blue) and the 100 highest (right, red) values of ΔA among 10,000 sets of rate constants for a network composed of four targets with [CaM] sampled in the range 1- 100 μM. Each spoke corresponds to the normalized log-scale range of the indicated rate constant in Fig. 2 and Table 2. Each set of rate constants is represented by a polygon whose vertices are defined by the values of the rate constants.



$$\Delta G_C + \Delta G_{C,P} = \Delta G_P + \Delta G_{P,C}$$

$$\Delta G_{C,N} + \Delta G_{CN,P} = \Delta G_{C,P} + \Delta G_{CP,N}$$

$$k_{2_j} = k_{7_j} \frac{k_{10_j}}{k_{9_j}} \frac{k_2}{k_1} \frac{k_{1_j}}{k_{8_j}}$$

$$k_{4_j} = k_{5_j} \frac{k_{8_j}}{k_{7_j}} \frac{k_4}{k_3} \frac{k_{3_j}}{k_{6_j}}$$

Figure S2. Thermodynamic cycles. The subscripts C and N indicate binding of Ca^{2+} to the C- and N-terminal domains of calmodulin (CaM), respectively. The subscript P indicates binding to target protein. Free energies of calcium binding and target binding are highlighted in blue and green, respectively.

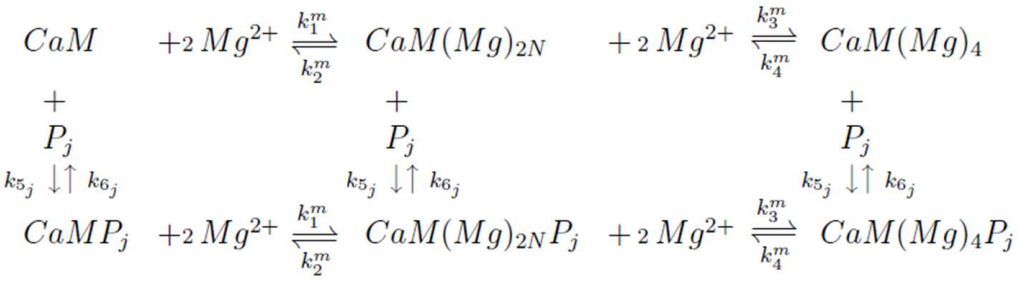


Figure S3. Reaction network for Mg^{2+}.

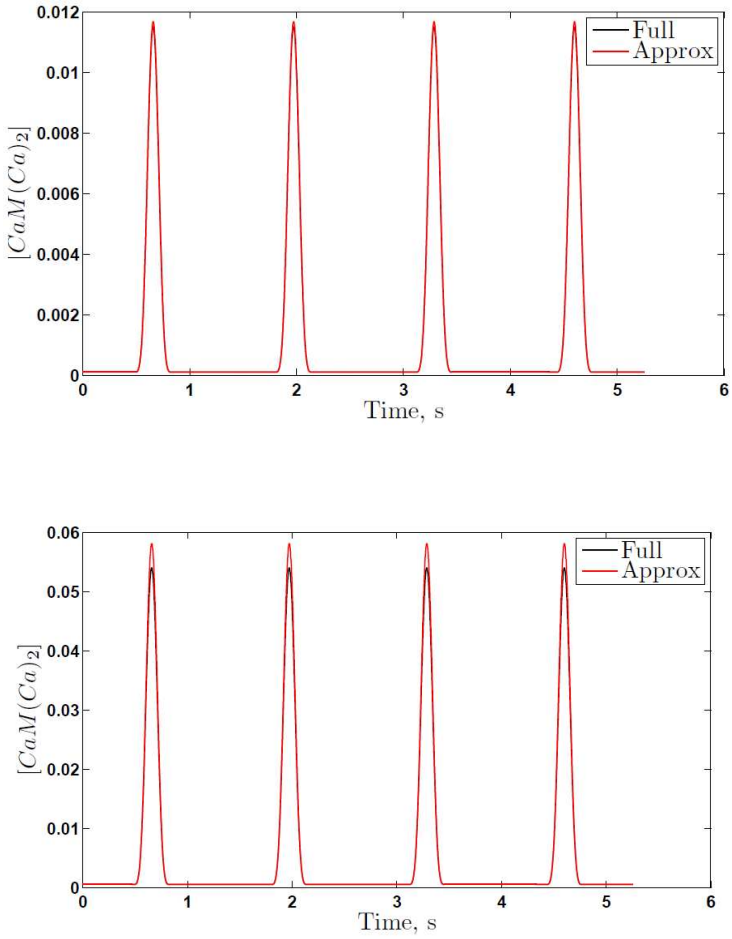


Figure S4. Approximating the association of two Ca^{2+} ions to a domain as a trimolecular reaction. These simulations were performed for a single 2-EF-hand calmodulin using either the trimolecular approximation (red) or the full model with separate rate constants for binding of the first and second calcium ion to the domain. The examples show results when the dissociation rate constant of Ca^{2+} from CaMCa is 5 times higher than from $CaM(Ca)_2$ (top) and when these rate constants are equal (bottom). The more typical scenario is that the difference is larger than 5 and then the models are indistinguishable.